

CLAIMS

1. A non-human transgenic mammal, characterized in that it comprises an IgH locus modified by replacing
5 the switch sequence S μ with all or part of a transgene consisting of the C α gene for a human class A immunoglobulin, including at least the exon encoding the CH3 domain and the membrane exon.
- 10 2. The non-human transgenic mammal as claimed in claim 1, characterized in that it is homozygous for said modified IgH locus.
- 15 3. The non-human transgenic mammal as claimed in claim 1 or claim 2, characterized in that said IgA locus is modified by replacing the switch sequence S μ with the entire C α gene.
- 20 4. The non-human transgenic mammal as claimed in claim 1 or claim 2, characterized in that said IgH locus is modified by replacing the switch sequence S μ with the segment of the C α gene including the exon encoding the CH3 domain and the membrane exon.
- 25 5. The non-human transgenic mammal as claimed in any one of claims 1 to 4, characterized in that said C α gene is C α 1.
- 30 6. The non-human transgenic mammal as claimed in any one of claims 1 to 5, characterized in that it comprises another transgene encoding a human immunoglobulin light chain.
- 35 7. The non-human transgenic mammal as claimed in claim 6, characterized in that said light chain is a kappa chain.

8. The non-human transgenic mammal as claimed in claim 7, characterized in that said transgene comprises the intronic activator E μ upstream and the palindrome *hs3a/hs1,2/hs3b* downstream.

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9. The non-human transgenic mammal as claimed in claim 8, characterized in that said transgene is under the control of the promoter of the human immunoglobulin heavy chain.

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10. The non-human transgenic mammal as claimed in any one of claims 6 to 9, characterized in that it is dizygous for said transgene.

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11. The non-human transgenic mammal as claimed in any one of claims 6 to 10, characterized in that it possesses an endogenous locus of the inactivated kappa chain.

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12. The non-human transgenic mammal as claimed in claim 11, characterized in that it is homozygous for said endogenous locus of the inactivated kappa gene.

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13. The non-human transgenic mammal as claimed in any one of claims 1 to 12, characterized in that it possesses a gene encoding the inactivated J chain.

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14. The non-human transgenic mammal as claimed in claim 13, characterized in that it is homozygous for said gene encoding the inactivated J chain.

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15. The non-human transgenic mammal as claimed in claim 13 or claim 14, characterized in that it comprises another transgene encoding a human immunoglobulin J gene.

16. The non-human transgenic mammal as claimed in any of claims 1 to 15, characterized in that it is a transgenic mouse.

17. A transgenic mouse as claimed in claim 16, characterized in that it comprises:

- 5 - an IgH locus modified by replacing the switch sequence S μ with the entire C α 1 gene for a human class A immunoglobulin, and
- 10 - a complete Vk gene comprising the rearranged VkI gene with a Jk5 gene, the Jk-Ck intron and the Ck gene, under the transcriptional control of the promoter of the human heavy chain (pVH), the intronic activator E μ upstream and the palindrome *hs3a/hs1,2/hs3b* downstream.

18. A homologous recombination targeting vector,
15 characterized in that it comprises the C α gene for a human class A immunoglobulin or a segment of this gene including at least the exon encoding the CH3 domain and the membrane exon, flanked by fragments of sequences of the IgH locus from a non-human mammal which are
20 adjacent to the S μ sequence.

19. The targeting vector as claimed in claim 18, characterized in that it comprises a cassette for expressing an appropriate selection marker, adjacent to
25 said C α gene or to a segment of said gene.

20. The targeting vector as claimed in claim 19, characterized in that said expression cassette is flanked by site-specific recombination sequences.

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21. The targeting vector as claimed in claim 19, characterized in that said sequences are LoxP sequences of the Cre recombinase.

35 22. The targeting vector as claimed in any one of claims 18 to 21, characterized in that said fragments of sequences which are adjacent to the S μ sequence are of murine origin.

23. The targeting vector as claimed in claim 22, characterized in that the C α gene or the segment of said gene is flanked, in 5' and in 3' respectively, by fragments corresponding to positions 131281 to 136441 and 140101 to 145032 in the sequence of murine chromosome 12 (accession number AC073553 in the EMBL/Genbank database).

24. An embryonic cell of a non-human mammal, modified with a targeting vector as claimed in any one of claims 18 to 23.

25. The use of a non-human transgenic mammal as claimed in any one of claims 1 to 16 or of a transgenic mouse as claimed in claim 17, for the production of humanized class IgA antibodies or of fragments of these antibodies.

26. A method for preparing humanized class IgA antibodies or fragments of these antibodies, characterized in that it comprises at least the following steps:

- the immunization of a non-human transgenic mammal as claimed in any one of claims 1 to 16 or of a transgenic mouse as claimed in claim 17, and,
- the production, by any appropriate means, of humanized class IgA antibodies or of fragments of these antibodies, from serum, secretions or B lymphocytes of said non-human transgenic mammal sacrificed beforehand.

27. A humanized class IgA antibody capable of being obtained by the method as claimed in claim 26, characterized in that it comprises a chimeric heavy chain in which the constant domains are of human origin and a human light chain in which the variable domain is encoded by V κ I-J κ 5.

28. A fragment of a humanized class IgA antibody as claimed in claim 27, characterized in that it comprises a fragment of said heavy and light chains.

5 29. The humanized class IgA antibody fragment as claimed in claim 28, characterized in that it is selected from the group consisting of the Fab, Fab'2 and Fc fragments.

10 30. A medicament, characterized in that it comprises a humanized class IgA antibody as claimed in claim 27 or a fragment of this antibody as claimed in claim 28 or claim 29.

15 31. A diagnostic reagent, characterized in that it comprises a humanized class IgA antibody as claimed in claim 27 or a fragment of this antibody as claimed in claim 28 or claim 29.

20 32. An immunogenic or vaccine composition, characterized in that it comprises at least one humanized class IgA antibody as claimed in claim 27 or a fragment of this antibody as claimed in claim 28 or claim 29, combined with an antigen.

25 33. A pharmaceutical composition, characterized in that it comprises at least one humanized class IgA antibody as claimed in claim 27 or a fragment of this antibody as claimed in claim 28 or claim 29, combined
30 by any appropriate means with an active ingredient.

34. The use of a humanized class IgA antibody as claimed in claim 27 or of a fragment of this antibody as claimed in claim 28 or claim 29, for the preparation
35 of a medicament intended for the prevention and treatment of infectious diseases and cancer.

35. The use of a humanized class IgA antibody as claimed in claim 27 or of a fragment of this antibody

as claimed in claim 28 or claim 29, for the preparation of a reagent intended for the diagnosis of infectious diseases and cancer.